In a preferred embodiment, the active compounds are prepared with carriers that will protect the compound against rapid elimination from the body, such as a controlled release formulation, including implants and microencapsulated delivery systems. Biodegradable, biocompatible polymers can be used, such as ethylene vinyl acetate, polyanhydrides, polyglycolic acid, collagen, polyorthoesters, and polylactic acid. Methods for preparation of such formulations will be apparent to those skilled in the art. The materials can also be obtained commercially from Alza Corporation and Nova Pharmaceuticals, Inc.

Liposomal suspensions (including liposomes targeted to infected cells with monoclonal antibodies to viral antigens) are also preferred as pharmaceutically acceptable carriers. These may be prepared according to methods known to those skilled in the art, for example, as described in U.S. Pat. No. 4,522,811 (which is incorporated herein by reference in its entirety). For example, liposome formulations may be prepared by dissolving appropriate lipid(s) (such as stearoyl phosphatidyl ethanolamine, stearoyl phosphatidyl choline, arachadoyl phosphatidyl choline, and cholesterol) in an inorganic solvent that is then evaporated, leaving behind a thin film of dried lipid on the surface of the container. An aqueous solution of the active compound or its monophosphate, diphosphate, and/or triphosphate derivatives are then introduced into the container. The container is then swirled by hand to free lipid material from the sides of the container and to disperse lipid aggregates, thereby forming the liposomal suspension.

IV. Preparation of Phosphate Derivatives of FTC

Mono, di, and triphosphate derivative of FTC can be prepared as described below.

The monophosphate can be prepared according to the procedure of Imai et al., *J. Org. Chem.*, 34(6), 1547–1550 (June 1969). For example, about 100 mg of FTC and about 280 μl of phosphoryl chloride are reacted with stirring in about 8 ml of dry ethyl acetate at about 0° C. for about four hours. The reaction is quenched with ice. The aqueous phase is purified on an activated charcoal column, eluting with 5% ammonium hydroxide in a 1:1 mixture of ethanol and water. Evaporation of the eluant gives ammonium FTC-5'-monophosphate.

The diphosphate can be prepared according to the procedure of Davisson et al., *J. Org. Chem.*, 52(9), 1794–1801 (1987). FTC diphosphate can be prepared from the corresponding tosylate, that can be prepared, for example, by reacting the nucleoside with tosyl chloride in pyridine at room temperature for about 24 hours, working up the product in the usual manner (e.g., by washing, drying, and crystallizing it).

The triphosphate can be prepared according to the procedure of Hoard et al., *J. Am. Chem. Soc.*, 87(8), 1785–1788 (1965). For FTC is activated (by making a imidazolide, according to methods known to those skilled in the art) and treating with tributyl ammonium pyrophosphate in DMF. The reaction gives primarily the triphosphate of the nucleoside, with some unreacted monophosphate and some diphosphate. Purification by anion exchange chromatography of a DEAE column is followed by isolation of the triphosphate, e.g., as the tetrasodium salt.

This invention has been described with reference to its preferred embodiments. Variations and modifications of the invention, will be obvious to those skilled in the art from the foregoing detailed description of the invention. It is intended that all of these variations and modifications be included within the scope of the appended claims.

We claim:

1. A method for treating HIV infection in humans comprising administering an effective amount of (−)-β-L-2-hydroxymethyl-5-(5-fluorocytosin-1-yl)-1,3-oxathiolane, or its physiologically acceptable salt, optionally in a pharmaceutically acceptable carrier.

2. The method of claim **1**, wherein the carrier is suitable for oral delivery.

3. The method of claim **1**, wherein the carrier comprises a capsule.

4. The method of claim **1**, wherein the carrier is in the form of a tablet.

5. The method of claim **1**, wherein the administration is parenteral.

6. The method of claim **1**, wherein β-L-2-hydroxymethyl-5-(5-fluorocytosin-1-yl)-1,3-oxathiolane is administered in a form that is at least 95% free of its corresponding β-D-enantiomer.

7. The method of claim **1**, wherein β-L-2-hydroxymethyl-5-(5-fluorocytosin-1-yl)-1,3-oxathiolane is administered in a form that is at least 95% free of its corresponding β-D-enantiomer.

8. The method of claim **1**, wherein β-L-2-hydroxymethyl-5-(5-fluorocytosin-1-yl)-1,3-oxathiolane is administered as an isolated enantiomer.

9. A method for treating HIV infection in humans comprising administering an effective amount of (+)-β-D-2-hydroxymethyl-5-(5-fluorocytosin-1-yl)-1,3-oxathiolane, or its physiologically acceptable salt, optionally in a pharmaceutically acceptable carrier.

10. The method of claim **9**, wherein the carrier is suitable for oral delivery.

11. The method of claim **9**, wherein the carrier comprises a capsule.

12. The method of claim **9**, wherein the carrier is in the form of a tablet.

13. The method of claim **9**, wherein the administration is parenteral.

14. The method of claim **9**, wherein β-D-2-hydroxymethyl-5-(5-fluorocytosin- 1-yl)-1,3-oxathiolane is administered in a form that is at least 95% free of its corresponding β-L enantiomer.

15. The method of claim **9**, wherein β-D-2-hydroxymethyl-5-(5-fluorocytosin-1-yl)-1,3-oxathiolane is administered in a form that is at least 95% free of its corresponding β-L-enantiomer.

16. The method of claim **9**, wherein β-D-2-hydroxymethyl-5-(5-fluorocytosin-1-yl)-1,3-oxathiolane is administered as an isolated enantiomer.

17. A method for treating HIV infection in humans comprising administering an effective amount of the monphosphate, diphosphate or triphosphate of β-L-2-hydroxymethyl-5-(5-fluorocytosin-1-yl)-1,3-oxathiolane, or its physiologically acceptable salt, optionally in a pharmaceutically acceptable carrier.

18. The method of claim **17**, wherein the phosphate of β-L-2-hydroxymethyl-5-(5-fluorocytosin-1-yl)-1,3-oxathiolane is administered in a form that is at least 95% free of its corresponding β-D-enantiomer.

19. The method of claim **17**, wherein the phosphate of β-L-2-hydroxymethyl-5-(5-fluorocytosin-1-yl)-1,3-oxathiolane is administered as an isolated enantiomer.

20. A method for treating HIV infection in humans comprising administering an effective amount of the monophosphate, diphosphate, or triphosphate of β-D-2-hydroxymethyl-5-(5-fluorocytosin-1-yl)-1,3-oxathiolane, or its physiologically acceptable salt, optionally in a pharmaceutically acceptable carrier.